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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/790,069 | 03/02/2004 | Chung-Liang Lin | 2410-0184P | 2563 |

2292 7590 09/15/2006

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| EXAMINER | |
|---|---|
| HENRY, MICHAEL C | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1623 | |

DATE MAILED: 09/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/790,069 | LIN ET AL. | |
| | Examiner | Art Unit | |
| | Michael C. Henry | 1623 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 1-24 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-24 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Claims 1-24 are pending in application

### *Claim Objections*

Claim 1 is objected to because of the following informalities: The claim recites the word "high" which appears to be a typographical error. It appears that the word "high" should be replaced by the word "highly". Appropriate correction is required.

Claim 1 is objected to because of the following informalities: The claim recites the phrase "strongly cation" which appears to contain a typographical error. It appears that the phrase "strongly cation" should be replaced by the phrase "strong cation". Appropriate correction is required.

Claim 7 is objected to because of the following informalities: The claim recites the word "large" which appears to be a typographical error. It appears that the word "large" should be replaced by the word "larger". Appropriate correction is required.

Claim 8 is objected to because of the following informalities: The claim recites the word "solving" which appears to be a typographical error. It appears that the word "solving" should be replaced by the word "dissolving". Appropriate correction is required.

Claim 15 is objected to because of the following informalities: The claim recites the phrase "by deionized water" which appears to contain a typographical error. It appears that the phrase "by deionized water" should be replaced by the phrase "with deionized water". Appropriate correction is required.

Claim 16 is objected to because of the following informalities: The claim recites the phrase "claim 16" which appears to contains a typographical error. It appears that the phrase

"claim 16" should be replaced by the phrase "claim 15". Appropriate correction is required. It should be noted that the claims are replete with typographical errors. Appropriate corrections are required.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the phrase "uses alcohol for precipitation" which renders the claim indefinite. More, specifically, it is unclear at which step is the alcohol used for precipitation and separation and whether the precipitation and separation occurs simultaneously. Furthermore, the claim fails clearly set forth the steps for carrying out the process and thus is indefinite.

The phrase "a step after the strongly cation exchange chromatography uses a solvent" in claim 5, render the claim indefinite. More specifically, it is unclear how said step uses the said solvent.

The phrase "a step after the immobilized enzyme affinity chromatography uses a solvent" in claim 6, render the claim indefinite. More specifically, it is unclear how said step uses the said solvent.

The phrase "is large than 95% (wt/wt) used to treat diabetes" in claim 7, render the claim indefinite. More specifically, it is unclear how diabetes is treated in the purification of acarbose.

The phrase "to be consistency by a concentration system" in claim 8, render the claim indefinite. More specifically, it is unclear what consistency of what system is being referred to.

The phrase "adding adequate ethyl alcohol to the consistency" in claim 8, renders the claim indefinite. More specifically, it is unclear what consistency of what system is being referred to.

The phrase "adding sodium chloride solution to eliminate an impurity" in claims 8 and 11, render the claims indefinite. More specifically, it is unclear how said impurity is eliminated.

The phrases "solving a sediment" and "solving a resin" in claim 8, render the claim indefinite. More specifically, it is unclear how said sediment or resin is solved.

The phrase "an upper liquid from an impure acarbose" in claim 15, renders the claim indefinite. More specifically, it is unclear what upper liquid is being referred to.

The phrase "solving a powder" in claim 19, renders the claim indefinite. More specifically, it is unclear how said powder is solved.

The phrase "by using a times distill water" in claim 19, renders the claim indefinite. More specifically, it is unclear what is a times distill water.

The phrase "solving an impure acarbose" in claim 23, renders the claim indefinite. More specifically, it is unclear how said impure acarbose is solved is solved.

It should be noted that the claims are replete with indefiniteness and uncertainties. And, the aforementioned indefiniteness and uncertainties are not the only ones in the claims.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hong et al. (US 6,649,755 B1) in view of Crueger et al. (US 5,989,882).

In claim 1, applicant claims "A purification process for manufacturing a high pure acarbose uses alcohol for precipitation and separation, a strongly cation exchange chromatography and an immobilized enzyme affinity chromatography for purification and purifying an acarbose-containing fermentation broth to get a high pure acarbose." Claim 2 is drawn to the purification process of claim 1, wherein the strong cation exchange chromatography uses a styrene divinylbenzene copolymer without methoxymethylmethacrylamide to be a resin matrix. Claim 3 is drawn to the purification process of claim 1, wherein the enzyme of the immobilized enzyme affinity chromatography uses $\alpha$–amyloglucosidase ($\alpha$-glucoamylase). Claims 4-7 are drawn to said purification process further use solvents, ammonia and distilled water and wherein the purity of the acarbose is larger than 95% (wt/wt).

Hong et al. disclose a purification process for manufacturing a highly pure acarbose (not less than 98%) that uses alcohol, a strong cation exchange chromatography for the purification purifying an acarbose-containing fermentation broth to get said highly pure acarbose (see claims 1-10 and col. 4, lines 24-47). Furthermore, Hong et al discloses that an absorbent based on a styrene divinylbenzene ion exchange resin can be used in the strong cation exchange chromatography (see col. 3, lines26-60). Hong et al. disclose that acidic or basic aqueous solution can be used as eluates (which includes the commonly used basic ammonia solution) (see col.1, lines 43-54).

The difference between applicants' claimed method and the method of Hong et al. is that Hong et al. do not disclose the use of immobilized enzyme affinity chromatography.

Crueger et al. disclose that immobilized enzyme affinity chromatography can be used for isolating (separating) and purifying acarbose from a culture broth (fermentation broth) (see col. 3, lines 5-8 and abstract).

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made to have used the process of Hong et al., to prepare highly pure acarbose to treat diabetes and to use immobilized enzyme affinity chromatography such as $\alpha$-amyloglucosidase affinity chromatography since Crueger et al. disclose that immobilized enzyme affinity chromatography can be used for isolating (separating) and purifying acarbose.

One having ordinary skill in the art would have been motivated, to have used the process of Hong et al., to prepare highly pure acarbose to treat diabetes and to use immobilized enzyme affinity chromatography such as $\alpha$-amyloglucosidase affinity chromatography since Crueger et al. disclose that immobilized enzyme affinity chromatography can be used for isolating (separating) and purinfying acarbose.

Claims 8-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hong et al. (US 6,649,755 B1) in view of Lawton et al. (WO 99/07720).

In claim 8, applicant claims "A purification process for purifying the acarbose comprising the steps of: eliminating myselium from an acarbose-containing fermentation broth by centrifugation; concentrating filtrate of the acarbose-containing fermentation broth to be consistency by a concentration system; adding adequate ethyl alcohol to the consistency and blending to be a solution; taking an upper liquid from the solution by centrifugating;

concentrating the upper liquid to be a consistency by the concentrating system; putting the consistency into ethyl alcohol to get a consistency liquid; taking a sediment from the consistency liquid by centrifugating and solving the sediment by water to get an impure acarbose solution; blending a strongly cation exchange resin with the acarbose solution to get a resin; using sodium chloride solution to eliminate an impurity in the resin; using ammonia solution to eliminate an impurity in the resin; and solving the resin with ammonia solution to get a high pure acarbose. Dependent claim 9 is drawn to the purification process as claim 8, wherein the eliminating myselium from acarbose-containing fermentation broth step could use a filter to replace centrifugating. Dependent claim 10 is drawn to a method of claim 8 wherein the purity of the highly pure acarbose is 60% (wt/wt). Claim 11 is drawn to a process for manufacturing a high pure acarbose comprising the steps of adjusting the pH value of an impure acarbose; adding an cation exchange resin into the impure acarbose to get a solution; blending the solution and taking an upper liquid; adding a strong cation exchange resin into the upper liquid to get a mixing solution; mixing and shaking the mixing solution to make the strong cation exchange resin absorbing acarbose; using sodium chloride solution to eliminate an impurity in the acarbose; and using ammonia solution to elute the acarbose to get a high pure acarbose. Claims 12-14 are drawn to the method of claim 12 wherein a strong cation exchange resin is used and wherein the purity of the acarbose is up to 78%

Hong et al. disclose a purification process for purifying the acarbose comprising eliminating myselium from an acarbose-containing fermentation broth by filtration; adding alcohol to the resulting pH adjusted solution to give an impure acarbose solution of not less than

50% purity of acarbose; contacting the acarbose solution with a strong cation exchange resin and eluting with distilled water to give high pure acarbose (see col. 4, lines 24-47 and claims).

The difference between applicants' claimed method and the method of Hong et al. is that Hong et al. do not disclose the use of sodium chloride solution or ammonia solution.

Lawton et al. disclose a process for the purification of acarbose comprising loading a prepurified acarbose solution on a chromatography column packed with a non-aromatic strong acid cation exchanger which is hydrophilic and has high mass transfer, followed by subsequent elution (see abstract). Furthermore, Lawton et al. purified acarbose has a purity of 98 % in dry matter (see page 6, example 1). In addition, Lawton et al. teach that the purity of the acarbose obtainable according to Lawton et al.' process is at least 98% (see page 5, lines 16 and 17). Lawton et al. also use ammonia solution ($NH_4OH$) (see example 1) as an eluting agent, and they also teach that sodium chloride (NaCl) can be used (see page 4, lines 12-15). It should be noted that it is common in the art to use centrifugation in place of filtration. In fact, applicant claims the use of a filter (filtration) to replace centrifugation (see claim 9). In addition, the examiner affords little weight to the mixing or blending of solutions or the concentrating of liquids, since the mixing of solutions or concentrating of liquids do not affect the purity of the resultant acarbose product.

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made to have used the process of Hong et al., to prepare highly pure acarbose to treat diabetes and to use ammonia solution and sodium chloride to purify the acarbose since Lawton et al. disclose that ammonia solution and sodium chloride can be used to purify the acarbose.

One having ordinary skill in the art would have been motivated, to have use the process of Hong et al., to prepare highly pure acarbose to treat diabetes and to use ammonia solution and sodium chloride to purify the acarbose since Lawton et al. disclose that ammonia solution and sodium chloride can be used to purify the acarbose.

In claim 15, applicant claims a purification process for manufacturing a high pure acarbose comprising the steps of: adjusting pll value of an upper liquid from an impure acarbose mixing a strong cation exchange resin; passing the upper liquid through a strong cation exchange resin column; washing the strong cation exchange resin in the column by deionized water till the absorbance of strong cation exchange resin being zero or steady; getting an impure acarbose by using ammonia solution to elute the strong cation exchange resin; concentrating the acarbose-containing fractions to be a volume by a concenteration system; and using alcohol for extracting the impure acarbose to get a high pure acarbose. Dependent claims 16-18 are drawn to said process involving specific flow velocity, the use of ammonia solution for eluting the acarbose and producing acarbose of up to 85% purity.

Hong et al. disclose a purification process for purifying the acarbose comprising eliminating myselium from an acarbose-containing fermentation broth by filtration; adding alcohol to the resulting pH adjusted solution to give an impure acarbose solution of not less than 50% purity of acarbose; contacting the acarbose solution with a strong cation exchange resin and eluting with distilled water to give high pure acarbose (see col. 4, lines 24-47 and claims).

The difference between applicants' claimed method and the method of Hong et al. is that Hong et al. do not disclose the use of sodium chloride solution or ammonia solution.

Lawton et al. disclose a process for the purification of acarbose comprising loading a prepurified acarbose solution on a chromatography column packed with a non-aromatic strong acid cation exchanger which is hydrophilic and has high mass transfer, followed by subsequent elution (see abstract). Furthermore, Lawton et al. purified acarbose has a purity of 98 % in dry matter (see page 6, example 1). In addition, Lawton et al. teach that the purity of the acarbose obtainable according to Lawton et al.' process is at least 98% (see page 5, lines 16 and 17). Lawton et al. also use ammonia solution ($NH_4OH$) (see example 1) as an eluting agent, and they also teach that sodium chloride (NaCl) can be used (see page 4, lines 12-15).

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made to have used the process of Hong et al., to prepare highly pure acarbose to treat diabetes and to use ammonia solution and sodium chloride to purify the acarbose since Lawton et al. disclose that ammonia solution and sodium chloride can be used to purify the acarbose.

One having ordinary skill in the art would have been motivated, to have use the process of Hong et al., to prepare highly pure acarbose to treat diabetes and to use ammonia solution and sodium chloride to purify the acarbose since Lawton et al. disclose that ammonia solution and sodium chloride can be used to purify the acarbose.

Claims 19-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hong et al. (US 6,649,755 B1) in view of Crueger et al. (US 5,989,882).

In claim 19, applicant claims a purification process for manufacturing a high pure

acarbose comprising the steps of: solving a powder of acarbose, which the purity is 83%-87%; by distilled water to be a solution; adjusting pH value of the solution; passing the solution through α-amyloglucosidase column; washing the α-amyloglucosidase column by using a times deionied water volume as the volume of the α-amyloglucosidase column; eluting an acarbose from the α–amyloglucosidase column by distilled water; concentrating the acarbose-containing fractions to be a volume by a concenteration system; and using alcohol for precipitating the impure acarbose to get a high pure acarbose. Dependent claims 20-24 are drawn to a process of claim 20 involving specific flow velocity washing the column with with deioned water, desolving an impure acarbose from said column and producing acarbose of purity up to 95%.

Hong et al. disclose a purification process for manufacturing a highly pure acarbose (not less than 98%) that uses alcohol, a strong cation exchange chromatography for purification and purifying an acarbose-containing fermentation broth to get said highly pure acarbose (see claims 1-10 and col. 4, lines 24-47). Furthermore, Hong et al discloses that an absorbent based on a styrene divinylbenzene ion exchange resin can be used in the strong cation exchange chromatography (see col. 3, lines26-60). Hong et al. disclose that acidic or basic aqueous solution can be used as eluates (which includes the commonly used basic ammonia solution) (see col.1, lines 43-54).

The difference between applicants' claimed method and the method of Hong et al. is that Hong et al. do not disclose the use of immobilized enzyme affinity chromatography.

Crueger et al. disclose that immobilized enzyme affinity chromatography can be used for isolating (separating) and purifying acarbose from a culture broth (fermentation broth) (see col. 3, lines 5-8 and abstract).

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made to have used the process of Hong et al., to prepare highly pure acarbose to treat diabetes and to use immobilized enzyme affinity chromatography such as $\alpha$-amyloglucosidase affinity chromatography since Crueger et al. disclose that immobilized enzyme affinity chromatography can be used for isolating (separating) and purifying acarbose.

One having ordinary skill in the art would have been motivated, to have used the process of Hong et al., to prepare highly pure acarbose to treat diabetes and to use immobilized enzyme affinity chromatography such as $\alpha$-amyloglucosidase affinity chromatography since Crueger et al. disclose that immobilized enzyme affinity chromatography can be used for isolating (separating) and purifying acarbose. It should be noted that examiner gives little weight to the flow velocity of the solvent through the column since said flow velocitiy does not appear to affect the purity of the acarbose produced.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Henry whose telephone number is 571-272-0652. The examiner can normally be reached on 8.30am-5pm; Mon-Fri. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael C. Henry

9/11/06

Shaojia Anna Jiang, Ph.D.
Supervisory Patent Examiner
Art Unit 1623

September 7, 2006.